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5. (Amended) A method of determining the identification of a nucleotide at a detection position in a target sequence comprising a first target domain comprising said detection position and a second target domain adjacent to said detection position, wherein said method comprises:

a) hybridizing a first ligation probe to said first target domain, said first ligation probe comprising:

i) an upstream universal priming site (UUP); and

ii) a first target-specific sequence comprising a first base at an interrogation position; and

b) hybridizing a second ligation probe to said second target domain, said second ligation probe comprising:

i) a downstream universal priming site (DUP); and

ii) a second target-specific sequence;

wherein if said first base is perfectly complementary to said nucleotide at said detection position, a ligation complex is formed wherein at least one of said first and second ligation probes comprises an adapter sequence;

c) removing non-hybridized probes;

d) providing a ligase that ligates said first and second ligation probes to form a ligated probe;

e) amplifying said ligated probe using said UUP and said DUP to generate a plurality of amplicons;

f) contacting said amplicons with an array of capture probes; and

g) determining the nucleotide at said detection position.

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9. (Amended) A method according to claim 5, 26, 32 and 33 wherein said removing comprises:

a) enzymatically adding a binding ligand to said target sequence to form a target sequence comprising said binding ligand;

b) binding a hybridization complex comprising said target sequence comprising said binding ligand to a binding partner immobilized on a solid support;

c) washing away unhybridized probes; and

d) eluting said probes off said solid support.

B6 12. (Amended) A method according to claim 11 wherein said support is a bead.

19. (Amended) A method according to claim 5 or 32, further comprising providing a support on which the target sequence is immobilized.

B7 20. (Amended) A method according to claim 19, wherein said non-hybridized probes are removed without removing said target sequence from said support.

21. (Amended) A method according to claim 5 or 32, further comprising attaching said target sequence to a support.

22. (Amended) A method according to claim 21, wherein said target sequence is attached to said support by a method selected from the group consisting of labeling said target sequence with a functional attachment moiety that binds said support, absorption of said target sequence on a charged support, direct chemical attachment of said target sequence to said support and photocrosslinking said target sequence to said support.

23. (Amended) A method according to claim 9, wherein said support is selected from the group consisting of paper, plastic and tubes.

B8 26. (Amended) A method of determining the identification of a nucleotide at a detection position in a target sequence comprising a first target domain comprising said detection position and a second target domain adjacent to said detection position, wherein said method comprises:

a) providing a support on which the target sequence is immobilized;

b) hybridizing a first ligation probe to said first target domain, said first ligation probe comprising:

i) an upstream universal priming site (UUP); and

ii) a first target-specific sequence comprising a first base at an interrogation position; and

c) hybridizing a second ligation probe to said second target domain, said second ligation probe comprising:

i) a downstream universal priming site (DUP); and

ii) a second target-specific sequence;

wherein if said first base is perfectly complementary to said nucleotide at said detection position, a ligation complex is formed and wherein at least one of said first and second ligation probes comprises an adapter sequence;

d) removing non-hybridized probes;

e) providing a ligase that ligates said first and second ligation probes to form a ligated probe;

f) amplifying said ligated probe with said UUP and said DUP to generate a plurality of amplicons;

g) contacting said amplicons with an array of capture probes; and

h) determining the nucleotide at said detection position.

30. (New) A method according to claim 9 wherein said solid support is a bead.

31. (New) A method according to claim 26 wherein said non-hybridized probes are removed without removing said target sequence from said support.

32. (New) A method of determining the identification of a nucleotide at a detection position in a target sequence comprising a first target domain comprising said detection position and a second target domain adjacent to said detection position, wherein said method comprises:

a) hybridizing a first ligation probe to said first target domain, said first ligation probe comprising:

i) an upstream universal priming site (UUP);

ii) a first target-specific sequence; and

iii) an interrogation position that is complementary to said detection position; and

b) hybridizing a second ligation probe to said second target domain, said second ligation probe comprising:

i) a downstream universal priming site (DUP); and

ii) a second target-specific sequence;

whereby if said interrogation position of said first probe is perfectly complementary to said nucleotide at said detection position, a ligation complex is formed, wherein at least one of said first and second ligation probes comprises an adapter sequence;

c) removing non-hybridized probes;

d) providing a ligase that ligates said first and second ligation probes to form a ligated probe;

e) amplifying said ligated probe using said UUP and said DUP to generate a plurality of amplicons;

f) contacting said amplicons with an array of capture probes; and

g) determining the nucleotide at said detection position.

33. (New) A method of determining the identification of a nucleotide at a detection position in a target sequence comprising a first target domain comprising said detection position and a second target domain adjacent to said detection position, wherein said method comprises:

a) providing a support on which the target sequence is immobilized;

b) hybridizing a first ligation probe to said first target domain, said first ligation probe comprising:

i) an upstream universal priming site (UUP);

ii) a first target-specific sequence; and

iii) an interrogation position; and

c) hybridizing a second ligation probe to said second target domain, said second ligation probe comprising:

i) a downstream universal priming site (DUP); and

ii) a second target-specific sequence;

whereby if said interrogation position of said first probe is perfectly complementary to said nucleotide at said detection position, a ligation complex is formed, and wherein at least one of said first and second ligation probes comprises an adapter sequence;

d) removing non-hybridized probes;

e) providing a ligase that ligates said first and second ligation probes to form a ligated probe;

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f) amplifying said ligated probe to generate a plurality of amplicons;

g) contacting said amplicons with an array of capture probes; and

h) determining the nucleotide at said detection position.

34. (New) A method according to claim 15, wherein said substrate comprises a fiber optic bundle.

REMARKS

Claims 5, 9-16, 19-23, and 26 are pending and claims 5, 9-16, 19-23, and 26 stand rejected in the instant application. The Examiner has acknowledged Applicant's election of Group II. Claims 30, 31, 32, 33, and 34 have been newly added. Support for this amendment can be found in the claims as filed and throughout the specification. No new matter has been added.

Oath/Declaration

Applicant would first like to thank the Examiner for the telephone conference of October 23, 2002. In the Office action, the Examiner states that the oath is defective, because the inventor Jian-Bing Fan did not sign his fill name. Applicants have enclosed a copy of the oath for the Examiner's convenience. Applicants note that Dr. Jian-Bing Fan did sign his full name. Accordingly, Applicants respectfully request that the objection be withdrawn.

Specification

With regard to comment one, the Brief Description of the Drawings has been amended to include descriptions of figures 1 through 6 at page 2, line 25. Support for these amendments is found in the figures 1 through 6 as filed.

With regard to comment two, the Brief Description of the Drawings has been amended to include a description of item 30 in figure 7 at page 3, line 2. Support for this amendment is found in figure 8, as well as on page 3, line 6 as filed.